85. (Reiterated) The method of claim 71, wherein said agent is administered in combination with other therapeutic agents.

86. (Reiterated) The method of claim 72 wherein said cell is a platelet.

87. (Reiterated) The method of claim 71 wherein said mammal is a human.

88. (Reiterated) The method of claim 71 wherein said agent is administered at a dose of from about 0.01 mg/kg to about 200 mg/kg of body weight.

89. (Reiterated) The method of claim 88 wherein said agent is administered at a dose of about 100 mg/kg of body weight.

REMARKS

Claims 71-73, 77-81 and 83-89 are currently pending in this application, and a complete set of the pending claims is reproduced above in accordance with the Examiner's suggestion. Although the Examiner has indicated in the Office Action that claims 71-74 and 76-85 are currently pending, applicants had submitted new claims 86-89 in the prior Amendment. Accordingly, these claims are reproduced above with the other pending claims for the Examiner's convenience.

Claims 71-81 and 83-85 stand rejected under 35 U.S.C. 112, first paragraph, because the specification is not enabling for any fragment or analog of PSGL. This ground of rejection is respectfully traversed.

Claim 71 has been amended to recite that the agent inhibits the interaction of P-selectin and PSGL-1 as suggested by the Examiner. Applicants submit that this amendment is effective to obviate the instant rejection as indicated by the Examiner in the Office Action.

Claims 71-82 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Cummings et al. (U.S. Patent No. 5,464,778). Claims 71-85 also stand rejected under 35 U.S.C. 103(a) as obvious over the Cummings et al. reference in view of Larsen et al. (U.S. Patent No. 5,840,679). These grounds of rejection are traversed.

The Examiner states that the Cummings et al. reference teaches the use of PSGL for the treatment of leukocyte adherence, inflammation and coagulation, including ischemia-reperfusion injury and atherosclerosis.

The present claims are directed to the use of PSGL-1, soluble forms of PSGL-1, fragments of PSGL-1, and mimetics of PSGL-1 to treat or inhibit atherosclerosis in a mammal. According to the method of the present invention, these agents can be administered to a mammal to inhibit the interaction between P-selectin and PSGL-1 and between E-selectin and a ligand of E-selectin. Statements to the contrary in the Office Action notwithstanding, atherosclerotic lesions are formed as a result of the binding of monocytes and T-lymphocytes to the surfaces of endothelial cells in the lumen of the artery wall. The monocytes become macrophages, accumulate lipids, and become foam cells. It is these cells, together with T-lymphocytes, that form lesions and fibrous plaques. This process is distinct from the leukocyte interactions associated with acute inflammatory conditions described in the Cummins et al. and Larsen et al. references. See pages 1 and 2 of the specification.

The Cummings et al. reference does state that platelet-leukocyte interactions **might** play a role in the recruitment of monocytes into atherosclerotic plaques. See col. 19, lines 65-66 of the reference. However, this is purely speculative on the part of the patentee, and there is no indication that the patentee seriously contemplated that the use of P-selectin ligand can be used to treat atherosclerosis.

Moreover, there is no disclosure in either Cummings et al. or Larsen et al. concerning the use of a P-selectin ligand to inhibit the interaction between P-selectin and PSGL-1 **and** E-selectin and a ligand of E-selectin. In this regard, the Examiner's attention is directed to the Declaration of Dr. Denisa Wagner, previously submitted in connection with the prosecution of this application, which explains in detail the nonobvious discovery concerning the use of PSGL-1 to inhibit both P-selectin and E-selectin binding.

Neither the Cummings et al. nor the Larsen et al. references recognize the role of P-selectin in the formation of atherosclerotic lesions, or teach or suggest the use of PSGL to prevent the formation of the lesions, i.e. to prevent atherosclerosis. Cummings et al. is directed to a novel ligand of P-selectin derived from myeloid cells. Cummings et al. teach that antibodies to the ligand can be used to block binding to the ligand on leukocytes, thus inhibiting inflammation.

Claims 71-85 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting in view of claims 40-41, 45, 49-52, 56, 59-60, and 73-74 of copending U.S. application no. 09/436,076, and claims 39-88 of U.S. application no. 09/883,642.

Applicant would be prepared to file a terminal disclaimer in this application to overcome this rejection provided that the application is otherwise considered to be in proper condition for allowance.

In view of the foregoing facts and reasons, the present application is now believed to overcome the remaining rejections, and to be in proper condition for allowance. Accordingly, reconsideration and withdrawal of the rejections, and favorable action on this application, is solicited. Entry of this amendment is deemed appropriate at this time since it serves to advance with prosecution of this application, and it does not require any further search or consideration on the part of the Examiner. The Examiner is invited to contact the undersigned at the telephone number listed below to discuss the status of this application.

Respectfully submitted,

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71. (Twice Amended) A method for treating or inhibiting atherosclerosis in a mammal comprising:

providing an agent for inhibiting an interaction between P-selectin and PSGL-1 [a ligand of P-selectin] and between E-selectin and a ligand of E-selectin; and

administering said agent to a mammal in need of such treatment so as to cause such inhibition to occur, wherein said agent is selected from the group consisting of PSGL-1, soluble forms of PSGL-1, fragments of PSGL-1, and mimetics of PSGL-1.